Table 1 - Quantitation of known interactors in a traditional Two-Hybrid Screen (2HS) and the novel Interaction Hybrid System (IHS) at various levels of sensitivity

BAIT HYBRID	LIBRARY HYBRID	TRADITIONAL 2HS	LOW SENSITIVITY IHS	MEDIUM SENSITIVITY IHS	HIGH SENSITIVITY IHS
SNF1	SNF4	300	50	250	2000
Pelle	Tube	250	20	150	1400
Pelle	Dorsal	1300	100	1400	2500

* All quantitations of interactions are in Miller units.

In the Drawing:

Please replace Drawing Sheet 1, Figure 1 and Drawing Sheet 2, Figures 2-4 with the replacements sheets attached hereto. Amendments are made to Figures 1 and 3.

In the Claims:

Please cancel Claims 3, 7, 14 and 15.

Please amend Claims 1, 4, 5, 8, 9, 11, 12, 16 and 17 as follows:

1.(once amended) A method for detecting an interaction between a first test protein and a second test protein at variable sensitivities via a detectable reporter gene, the method comprising:

(a) providing a host cell wherein the host cell comprises a detectable reporter gene capable of expressing a detectable reporter gene product;

(b) providing to the host cell a first hybrid protein comprising a polypeptide region capable of binding DNA and a bait polypeptide derived from the first test protein and a second hybrid protein comprising a polypeptide

region capable of transcriptional activation and a prey polypeptide derived from the second test protein, wherein the host cell is additionally provided with the capacity to regulate the absolute or relative amounts of the first and second hybrid proteins;

(c) regulating the amounts of the first and second hybrid proteins in a continuously adjustable manner so the detectable reporter gene is activated; and

(d) determining the extent to which the detectable reporter gene has been activated.

4.(once amended) The method of Claim 1, wherein the first or second hybrid protein is provided by introducing into the host cell a first or second chimeric gene capable of being expressed in the host cell.

5.(once amended) The method of Claim 4, wherein the first chimeric gene comprises a first exogenously activatable promoter, a sequence coding for a DNA binding region or polypeptide, and a sequence coding for the bait polypeptide.

8.(once amended) The method of Claim 4, wherein the second chimeric gene comprises a second exogenously activatable promoter, a sequence coding for a transcriptional activation domain or polypeptide, and a sequence coding for the prey polypeptide.

9.(once amended) The method of Claim 8, wherein the second exogenously activatable promoter is activated by a second exogenous activator.

11.(once amended) The method of Claim 10, wherein at least one of the first or second exogenous activators is chosen from the group consisting of cortisol, hydrocortisone, estrogen, estradiol, estrone, progesterone, androgen, ecdysone, retinoid, steroids which bind to orphan receptors, mineralocorticoid and mineralocorticoid analogues.

12.(once amended) The method of Claim 1, additionally comprising rendering the host cells capable of regulating the relative or total amounts of the first or second hybrid proteins in response to a modulatory agent acting at one or more of an extracellular, membrane, intracellular or nuclear site in order to provide continuous adjustment of a selected reporter sensitivity, wherein the modulatory agent consists of at least one of:

(a) a natural or synthetic, metabolically active or inactive steroid, steroid analogue or steroid mimic;

(b) a membrane-active agent or analogue thereof;

(c) a small molecular pharmaceutical agent;

(d) a biomolecule or natural or synthetic biopharmaceutical.

16.(once amended) The method of Claim 12, wherein an agent capable of interfering with function of the modulatory agent is added to regulate the relative or absolute amounts of the first or second hybrid proteins.

17.(once amended) The method of claim 1, wherein the host cell is from a *Saccharomyces cerevisiae* strain comprising three integrated reporters for the detection of two-hybrid interactions, the first integrated reporter being a construct yielding a quantifiable product, the second and third integrated reporters being constructs yielding proteins sufficient to rescue nutrient auxotrophies; wherein the first hybrid protein is provided by

(a) introducing into the host cell a plasmid containing an ampicillin or kanamycin resistance gene, a colE1 origin of replication and a DNA sequence encoding a first hybrid protein comprising a bait polypeptide and a Gal4p DNA binding domain, the expression of which is controlled by an integrated estrogen-inducible promoter; then

(b) inducing expression of the first hybrid protein by incubating the host cell with an exogenous activator capable of activating the promoter; and wherein the second hybrid protein is provided by

(a) introducing into the host cell a plasmid containing an ampicillin or kanamycin resistance gene, a colE1 origin of replication and a DNA sequence encoding a second hybrid protein comprising a prey polypeptide derived from a library and the carboxyl-terminal end of the Gal 4p transcriptional activation domain, the expression of which is controlled by a rat glucocorticoid-inducible promoter; then

(b) inducing expression of the second hybrid protein by incubating the host cell with an exogenous activator capable of activating the promoter.

Please add new Claims 18-21 as follows:

18.(new) The method of Claim 12, wherein the natural or synthetic, metabolically active or inactive steroid, steroid analogue or steroid mimic is selected from the group consisting of glucocorticoids, dexamethasone, cortisone, cortisol, hydrocortisone, estrogens, estradiol, estrone, progesterones, androgens, ecdysones, and steroids which bind to orphan receptors, and mineralocorticoid or mineralocorticoid analogues.

19.(new) The method of Claim 12, wherein the membrane-active agent or analogue thereof, is selected from the group consisting of an ionophore, an anesthetic agent, a detergent, an amphoteric agent, a hydrophobic agent, a lipid-active agent, a solvent, a transmembrane signaling agent, an intramembrane signaling agent, and a farnesylating agent.

20.(new) The method of Claim 12, wherein the small molecular pharmaceutical agent is selected from the group consisting of antimicrobial agents, anti-tumor agents, nucleic-acid binding agents, cytoskeletal active agents, chelators, inducers, co-repressors, and agents affecting intracellular trafficking, localization, protection and degradation of exogenous or endogenous mediators, hormones and molecules.

21.(new) The method of Claim 12, wherein the biomolecule or natural or synthetic biopharmaceutical is selected from the group consisting of growth factors, retinoids, cytokines, hormones, and their cellular receptors and fragments and mimetics thereof.